

CLAIMS

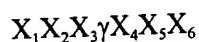
We claim:

1. In a polyamide having a hairpin turn derived from γ -aminobutyric acid which specifically binds to base pairs in the minor groove of a DNA molecule, the improvement comprising substitution of the γ -aminobutyric acid residue of the hairpin with (R)-2,4-diaminobutyric acid.

2. A polyamide of claim 1 wherein the R-2-amino is derivatized to form an acid amide.

3. A polyamide of claim 1 wherein the polyamide has three or four carboxamide binding pairs.

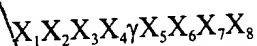
4. A polyamide of claim 1 having the formula:



wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_2 , X_3/X_4 , and X_5/X_6 represent three carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound.

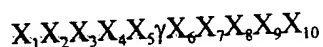
5. A polyamide of claim 1 having the formula:



wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_8 , X_2/X_7 , X_3/X_6 , and X_4/X_5 represent four carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound.

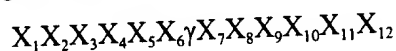
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6. A polyamide of claim 1 having the formula:



10 wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_{10} , X_2/X_9 , X_3/X_8 , X_4/X_7 , X_5/X_6 represent five carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound.

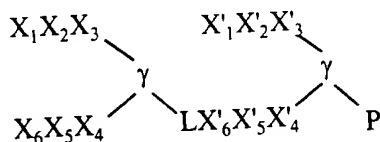
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7. A polyamide of claim 1 having the formula:



20 wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

25 X_1/X_{12} , X_2/X_{11} , X_3/X_{10} , X_4/X_9 , X_5/X_8 , X_6/X_7 represent three or four carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound.

8. A tandem-linked polyamide of claim 1 having the formula:



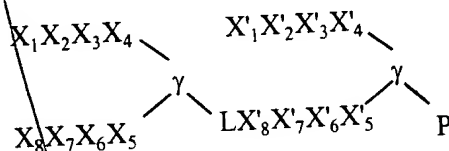
wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_6 , X_2/X_5 , X_3/X_4 , X'_1/X'_6 , X'_2/X'_5 , X'_3/X'_4 represent carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β -alanine and 5-aminovaleric acid (δ);

P represents zero to ten improved polyamides of claim 1.

9. A tandem-linked polyamide of claim 1 having the formula:



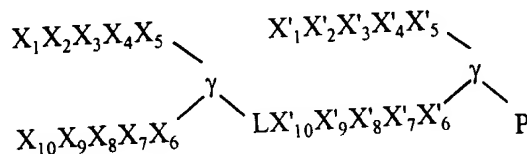
wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_8 , X_2/X_7 , X_3/X_6 , X_4/X_5 , X'_1/X'_8 , X'_2/X'_7 , X'_3/X'_6 , X'_4/X'_5 represent carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof; and,

P represents zero to ten improved polyamides of claim 1.

10. A tandem-linked polyamide of claim 1 having the formula:



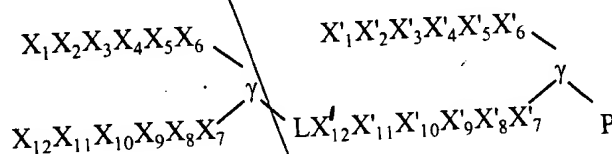
wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_{10} , X_2/X_9 , X_3/X_8 , X_4/X_7 , X_5/X_6 , X'_1/X'_{10} , X'_2/X'_9 , X'_3/X'_8 , X'_4/X'_7 , X'_5/X'_6 represent carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof; and,

P represents zero to ten improved polyamides of claim 1.

11. A tandem-linked polyamide of claim 1 having the formula:



wherein γ is $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$ hairpin linkage derived from γ -aminobutyric acid or a chiral hairpin linkage derived from R-2,4-diaminobutyric acid;

X_1/X_{12} , X_2/X_{11} , X_3/X_{10} , X_4/X_9 , X_5/X_8 , X_6/X_7 , X'_1/X'_{12} , X'_2/X'_{11} , X'_3/X'_{10} , X'_4/X'_9 , X'_5/X'_8 and X'_6/X'_7 represent carboxamide binding pairs which bind DNA base pairs wherein at least one binding pair is Hp/Py or Py/Hp and the other is selected

from the group consisting of Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof; and,

P represents zero to ten improved polyamides of claim 1.

12. A tandem-linked polyamide comprising a first and second polyamide wherein said first polyamide is a polyamide of claim 4 and said second polyamide is selected from the group consisting of a polyamide of claim 5, 6 and 7; said first and second polyamides being linked by an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof bound to the γ -residue of said first polyamide and the carboxy tail of said second polyamide.

13. A tandem-linked polyamide comprising a first and second polyamide wherein said first polyamide is a polyamide of claim 5 and said second polyamide is selected from the group consisting of a polyamide of claim 4, 6 and 7; said first and second polyamides being linked by an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof bound to the γ -residue of said first polyamide and the carboxy tail of said second polyamide.

14. A tandem-linked polyamide comprising a first and second polyamide wherein said first polyamide is a polyamide of claim 6 and said second polyamide is selected from the group consisting of a polyamide of claim 4, 5, and 7; said first and second polyamides being linked by an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (δ) and a derivative thereof bound to the γ -residue of said first polyamide and the carboxy tail of said second polyamide.

15. A tandem-linked polyamide comprising a first and second polyamide wherein said first polyamide is a polyamide of claim 7 and said second polyamide is selected from the group consisting of a polyamide of claim 4, 5, and 6; said first and second polyamides being linked by an amino acid linking group selected from the group consisting of β -alanine, 5-aminovaleric acid (8) and a derivative thereof bound to the γ -residue of said first polyamide and the carboxy tail of said second polyamide.

16. A tandem-linked polyamide of claims 8, 9, 10 or 11 wherein P represents zero to eight polyamides of claim 1.

17. A tandem-linked polyamide of claims 8, 9, 10 or 11 wherein P represents zero to six polyamides of claim 1.

18. A tandem-linked polyamide of claims 8, 9, 10 or 11 wherein P represents zero to four polyamides of claim 1.

19. A tandem-linked polyamide of claims 8, 9, 10 or 11 wherein P represents zero to two polyamides of claim 1.

20. A polyamide of claim 1 wherein said chiral hairpin linkage derived from R-2,4-diaminobutyric acid.

21. A polyamide of claim 1 selected the group consisting of:

ImPyPy- γ -PyPyPy- β -Dp;

ImPyPy-(R)^{H₂N₂} γ -PyPyPy- β -Dp;

ImPyPy-(S)^{H₂N₂} γ -PyPyPy- β -Dp;

ImPyPy-(R)^{H₂N₂} γ -PyPyPy- β -EtOH;

ImPyPy-(R)^{Ac} γ -PyPyPy- β -Dp;

ImPyPy-(S)^{Ac} γ -PyPyPy- β -Dp;

~~ImPyPy-(R)[ImPyPy-(R)^{H2N}γ-PyPyPy-β-]^{HN}γ-PyPyPy-β-Dp;
 ImPyPy-(R)[ImPyPy-(R)^{H2N}γ-PyPyPy-δ-]^{HN}γ-PyPyPy-β-Dp;
 ImPyPy-(R)[ImPyPy-(R)^{EDTA}γ-PyPyPy-δ-]^{HN}γ-PyPyPy-β-Dp; and,
 the pharmacologically acceptable salts thereof.~~

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22. A polyamide of claim 1 further comprising an R-2 amino group attached to a detectable label.
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23. A method of increasing the affinity polyamide having a hairpin turn for binding a DNA sequence comprising substituting the α-position of the γ-aminobutyric acid with (R)-2,4-diaminobutyric acid
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24. A method of claim 8 wherein the α-position of the γ-aminobutyric acid residue of the hairpin is substituted with an acetylated R-enantiomer of aminobutyric acid.
25. A method of inhibiting gene expression comprising contacting a regulatory sequence of a gene with a polyamide of claim 1.

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